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**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

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| JAN BUCH ET AL | ART UNIT: 1617 |
| SERIAL NO: 09/512,914 | EXAMINER: S. A. Jiang |
| FILED: FEBRUARY 25, 2000 | |
| FOR: THERAPEUTIC COMBINATION | |

Commissiner for Patents
Washington, D.C. 20231

**Supplemental Information Disclosure Statement**

Supplemental to the prior Information Disclosure Statement filed in this application on February 25, 2000, applicants wish to advise the Examiner regarding certain matters which may be of interest. Applicants also have listed some additional documents on the attached Information Disclosure Statement form ("IDS") for consideration (along with those previously listed on earlier IDS's).

The present application claims, inter alia, the administration to a defined patient population of two specific active ingredients, amlodipine and atorvastatin, for treatment of certain indicated conditions.

The administration of amlodipine and atorvastatin together is presently part of a large scale cardiovascular morbidity/mortality trial being conducted in the UK, Sweden and other foreign countries. This study, known as the Anglo Scandinavian Cardiac Outcomes Trial or ASCOT, involved approximately 18,000 patients at the start, and is funded by Pfizer, Inc.,

("Pfizer"), the assignee of the present application. The ASCOT study has been underway for some years but the final results are not expected for several more years.

A formal and widespread announcement of ASCOT occurred in May 1997. Professor Peter Sever of Imperial College, London, England presented certain posters describing ASCOT at the WHO/ISH Blood Pressure Lowering Treatment Trialists' Collaboration Symposium in St. Jean Cap Ferrat, France at that time. Copies of Dr. Sever's May 1997 posters are submitted as item A on the accompanying IDS. One of the posters lists as a "Tertiary Objective" of ASCOT the evaluation of "synergistic effects on total coronary or CV events" from "the use of atorvastatin and amlodipine".

Also attached to the present IDS is a press release by Pfizer dated May 20 1997, which formally announced the ASCOT trial and excerpts from a Press Kit which was also made available in May 1997 (item G).

None of this activity in May 1997 occurred more than one year prior to the effective filing date of the instant application (i.e., August 29, 1997).

On July 3, 1996, the British Hypertension Society ("BHS"), St. John's College, Cambridge, England notified its members by letter that at its annual meeting to be held in September 1996, Prof. P.S. Sever would make a presentation about ASCOT. The letter to BHS members described Dr. Sever's planned presentation as follows:

> "NEW SESSIONS:
>
> Two additional sessions will take place at this year's meeting:
>
> Anglo-Scandinavian Cardiac Outcome Trial (ASCOT) – the final solution to the BHS major morbidity-mortality trial – Professor P.S. Sever
>
> After several years of planning a BHS outcome trial in hypertension, it became apparent that obtaining full sponsorship for such a trial would only be possible if the trial was to become international. We are pleased to announce that a

> collaborative venture with Scandinavian colleagues for a trial very similar in design to the original BHS model has now been agreed and will be sponsored by Pfizer International. Representatives of the BHS will play a key role in ensuring that this is a highly successful venture and of great importance to the BHS as a Society.
>
> A formal presentation by Professor Peter Sever, followed by discussion, will take place from 7:00-8:00 p.m. on Monday 16th September in the Palmerston Lecture Theatre at St. Jon's College (preceded by drinks from 6:30 p.m.). All BHS and NHA members and their guests are welcome to attend. A buffet supper will be available in the Dining Hall from 8:00 p.m. – 9:30 p.m."

It will be noted that although the letter to BHS members mentioned ASCOT and its broad purpose (and its sponsorship by Pfizer), no disclosure was made in that letter that atorvastatin and/or amlodipine were among the drugs to be included in the study. Thus, no matter how the July 3, 1996 letter may be viewed (i.e., even if it were deemed to qualify as prior art under some subsection of 35 U.S.C. §102), it does not anticipate or render obvious the present claims. Professor Sever's later presentation to BHS members on September 16, 1996 (which did identify amlodipine and atorvastatin as drugs to be included in ASCOT and likely used posters similar to those provided as item A to the IDS) was given less than a year prior to the effective filing date of the instant application and the presentation was not made in the United States. A copy of the BHS letter of July 3, 1996 is attached as item J on the accompanying IDS.

While the above-mentioned press release, Press Kit, and Professor Sever's posters all represent activities prior to the effective filing date of the instant application (but less than a year earlier), they do not qualify as prior art to the instant claims at least because their description of the use of amlodipine and atorvastatin in ASCOT is not a description of an invention of "another" (i.e., these materials describe the inventions of Jan Buch and/or Rob Scott, the named inventors on the instant application, which is assigned to Pfizer, the company which sponsored and funded ASCOT). Under well-established authority, therefore, these non-statutory bar activities, even if deemed to be "prior art" under 35 U.S.C. §102 such as a printed publication

(and at least the Press Kit and press release seemingly would so qualify), are not the description of an invention by "another". See In re Katz, 215 USPQ 14, 17 (CCPA 1982) and Ex parte Lemieux, 115 USPQ 148 (B.P.A.I. 1957). As the Court explained in In re Katz (at 215 USPQ 17):

> "Thus, one's own work is not prior art under §102(a) even though it has been disclosed to the public in a manner or form which otherwise would fall under §102(a). Disclosure to the public of one's own work constitutes a bar to the grant of a patent claiming the subject matter so disclosed (or subject matter obvious therefrom) only when the disclosure occurred more than one year prior to the date of the application, that is, when the disclosure creates a one-year time bar, frequently termed a "statutory bar," to the application under §102(b). As stated by this court in In re Facius, 56 CCPA 1348, 1358, 408 F.2d 1396, 1406, 161 USPQ 294, 302 (1969), 'But certainly *one's own invention*, whatever the form of disclosure to the public, may not be prior art against oneself, *absent a statutory bar.*' [Emphasis in original.][2]
>
> "[2]Since any valid rejection is necessarily a 'statutory bar,' in a generic sense, the expression 'statutory bar' must be understood here as meaning 'statutory *time* bar' under 35 USC 102(b)." [Emphasis in original]

With regard to the origination of the combination of amlodipine and atorvastatin for use in ASCOT, applicants set forth a brief summary of the events based on an extensive investigation conducted by counsel.

In the late 1980's and early 1990's several organizations in the UK and Sweden (and Pfizer employees as well) proposed various studies to assess the long-term effects on coronary heart disease of different antihypertensive regimens, cholesterol lowering agents and antiplatelet therapy. Such proposals included a December 3, 1993 proposal by BHS identified as item C on the instant IDS. Among the drug combinations suggested for evaluation were a statin (unspecified) and a calcium channel blocker (e.g., amlodipine).

Funding for such extensive tests was unavailable at the time and thus actual studies were not undertaken. Other test proposals for anti-atherosclerotic effects were made, including the use

of amlodipine as a calcium channel blocker together with a statin (e.g., lovastatin and simvastatin).

Some results from smaller tests using calcium channel blockers and statins were published (see, for example, references previously cited and items D and E of the attached IDS).

Ultimately, Pfizer agreed to fund a broad study provided that researchers in the UK (headed by Dr. Peter Sever) and Sweden (headed by Drs. Bjorn Dahlöf and Hans Wedel) combined forces to conduct and evaluate the study. Dr. Jan Buch of Pfizer, together with other Pfizer representatives, had been and remained intimately involved in the organization of the proposed trial (now called ASCOT) and in the creation of a suitable testing protocol and the selection of the drugs (e.g., β-blocker, diuretic, statin, and ACE inhibitor) that would be used. While it was generally agreed that amlodipine would be one of the several drugs used in ASCOT, no immediate selection of the statin was made. The statin issue was up in the air, although simvastatin apparently was mentioned as an early possibility.

The suggestion of atorvastatin for use in ASCOT was first recorded in notes and minutes of a study meeting held in the UK attended by Drs. Buch, Sever, Dahlöf, and Wedel, together with other Pfizer personnel. This statin choice was confirmed in the minutes of a later ASCOT study meeting held about a month later. While a subsequent Pfizer document written a few months thereafter stated that atorvastatin was originally proposed by the British Hypertension Society as a possible comparative agent in ASCOT, counsel have investigated the true origin of this proposal and have concluded that the suggestion actually was based on the information and proposal provided to Dr. Sever by Dr. Jan Buch, one of the named inventors on the instant application.

Counsel has interviewed the attendees at the first ASCOT meeting where atorvastatin was mentioned, considered the minutes and notes which first record atorvastatin as the statin to be employed in ASCOT (together with amlodipine), and reviewed the underlying documentation, including records in both the United States and abroad. Based on this investigation, the first proposal to use atorvastatin as the statin in ASCOT (and thus, in accord with the ASCOT protocol, together with amlodipine) was made by Dr. Jan Buch and not by the British Hypertension Society (e.g., Dr. Peter Sever). Dr. Buch was the originator of the combination of amlodipine and atorvastatin and he is properly named as an inventor on the instant application together with Dr. Rob Scott, a co-worker at Pfizer who contributed to other aspects of the subject matter claimed.

Applicants respectfully submit that their prior amendment responding to the restriction/election requirements places this application in condition for allowance, and such action is earnestly solicited.

Respectfully submitted,
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